UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/461,938	12/15/99	LIAO	S 1279-293/099

HM22/0828

MARGARET A CHURCHILL
FULBRIGHT & JAWORSKI LLP
865 SOUTH FIGUEROA STREET
SUITE 28TH FLOOR
LOS ANGELES CA 90017

EXAMINER	
HUNT, J	
ART UNIT	**PAPER NUMBER**
1642	3

DATE MAILED: 08/28/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/461,938	Liao et al.
Examiner	**Group Art Unit**
Jennifer Nichols, Nee Hunt	1642

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-12 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-12 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 2

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- *SEE OFFICE ACTION ON THE FOLLOWING PAGES* ---

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-12 are unclear in the recitation of "significant lesions". The metes and bounds of significant lesions cannot be determined. Although applicant has specified 3 embodiments included in the scope of significant lesions, applicant fails to provide any guidance as to what qualities or properties allow the determination of a significant lesion. Therefor it is not possible to determine what lesions would be considered significant and what lesions would not.

Claims 8-12 are unclear in the recitation of "a characterizing fraction". The metes and bounds of a characterizing fraction cannot be determined. It is not clear what would be considered a characterizing fraction and what would not. For the purpose of examination, a "characterizing fraction" will be determined to mean any fraction of MN/CA IX to which an anti-MN/CA IX antibody will bind, thus allowing detection and subsequent determination of MN/CA IX. In light of this interpretation, claims 8-10 are improper because they are of identical scope to

claim 6. Specifically, all MN/CA IX antigens would be characterizing fractions and all characterizing fractions would be MN/CA IX antigens.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-10 and 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for detection of MN/CA IX antigen using antibody detection and immunohistochemical staining, and corresponding correlation to grade of cervical disease , does not reasonably provide enablement for detection of MN/CA IX antigen using any and all methods of MN/CA IX detection, including amplification and in situ hybridization, and corresponding correlation to grade of cervical disease . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining scope and enablement are: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented in the specification, 3) the presence or absence of working examples, 4) the nature of the invention, 5) the state of the prior art, 6) the relative skill of those in the art, 7) the predictability of the unpredictability of the art, and 8) the breadth of the claims (see Ex parte Forman, 230 USPQ 546, BPAI, 1986).

The claims broadly encompass any and all methods of detection of MN/CA IX antigen expression, including amplification and in situ hybridization, and subsequent correlation of this detection and staining patterns to cervical disease stage. The specification discloses a very specific immunohistochemical assay for MN/CA IX, using a solitary antibody which reacts with a singular epitope of MN/CA IX, and correlation of this antibody's staining patterns to cervical cancer stage. Applicant fails to provide any examples of detection of MN/CA IX using amplification and in situ hybridization. Further, applicant fails to provide any guidance or objective evidence that amplification and in situ hybridization would function in a similar manner for detection as the instant singular antibody/immunohistochemical staining embodiment does. Disclosure of one singular immunohistochemical embodiment is insufficient support under 112 first paragraph for claims which encompass any and all methods of detection, including amplification and in situ hybridization, particularly when said correlations are dependent on evaluation of said immunohistochemical staining patterns, and there is no evidence or teachings which would suggest that amplification and in situ hybridization would produce similar patterns and results.

Therefor one of ordinary skill in the art would not have been enabled to practice the invention commensurate in scope with the claims absent undue experimentation.

5. Claims 2 and 8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the

art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to methods which recite diagnosing a benign lesion when MN/CAIX antigen is not detected.

The specification provides no guidance or objective evidence that absence of MN/CA IX antigen permits diagnosis of a benign lesion. Although the specification and the prior art clearly sets forth the positive correlation of MN/CA IX expression and cervical dysplasia or cancer, the negative correlation between lack of MN/CA IX and lack of a malignant condition is not clear. Disclosure that the presence of a particular antigen is indicative of disease does not provide support for claims which recite that the absence of said antigen is indicative of a disease free state. Furthermore, the art teaches that not all MN/CA IX negative cases correlate with a benign condition. For example, Liao et al., Cancer Epidemiology and Biomarkers, Volume 5, pages 549-557, 1996, IDS Document #27 teaches in the abstract a case of an MN/CA IX negative case which squamous intraepithelial lesions were found in the cervix (see abstract). See also for example, table 1 of Liao et al., American Journal of Pathology, Volume 145, Number 1, pages 598-609, 1994, IDS #26, which discloses numerous MN/CA IX negative cases which were not benign conditions. Therefor one of ordinary skill in the art would not be enabled to practice the invention as claimed.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-11 are rejected under 35 U.S.C. 102(b) as anticipated by Liao et al., Cancer Epidemiology and Biomarkers, Volume 5, pages 549-557, 1996, IDS Document #27.

Liao et al. teaches a method for determining the presence of cancerous or pre-cancerous cervical lesions from histological tissue sections comprising cells that have been cytologically diagnosed as atypical glandular cells of undetermined significance (AGUS) under the Bethesda System of terminology, said Pap smear including atypical and normal endocervical cells, said method comprising subjecting said AGUS cells to a procedure whereby expression of MN/CA IX antigen is detected, observing the distribution of MN/CA IX antigen expressed on the atypical or normal cells of said AGUS cytologically diagnosed cells. The method further comprising diagnosing the presence of adenocarcinoma, invasive adenocarcinoma, or high grade squamous epithelial lesions (HAIL) when said MN/CA IX antigen is expressed on atypical cells, including a honeycomb pattern of distribution in adenocarcinoma and invasive adenocarcinoma and a tight cluster pattern of distribution in HAIL, diagnosing the presence of low grade squamous epithelial lesions (LSIL) or atypia when said MN/CA IX antigen is absent from atypical cells but present in morphologically normal cells, and diagnosing a benign condition when MN/CA IX antigen is absent. (See entire document, including figures)

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1-11 are rejected under 35 U.S.C. 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Liao et al., American Journal of Pathology, Volume 145, Number 1, pages 598-609, 1994, IDS #26.

Liao et al.(#26) teaches a method for determining the presence of cancerous or pre-cancerous cervical lesions including atypical and normal endocervical cells, said method comprising subjecting said cells to a procedure whereby expression of MN/CA IX antigen is detected, observing the distribution of MN/CA IX antigen expressed on the atypical or normal cells of said cytologically diagnosed cells. The method further comprising diagnosing the presence of adenocarcinoma, invasive adenocarcinoma, or high grade squamous epithelial lesions (HSIL) when said MN/CA IX antigen is expressed on atypical cells, including a honeycomb pattern of distribution in adenocarcinoma and invasive adenocarcinoma and a tight cluster pattern of distribution in HAIL, diagnosing the presence of low grade squamous epithelial lesions (LSIL) or atypia when said MN/CA IX antigen is absent from atypical cells but present in morphologically normal cells, and diagnosing a benign condition when MN/CA IX antigen is

absent. Although the document does not specifically recite that the sample is from Pap smear cells that have been cytologically diagnosed as atypical glandular cells of undetermined significance (AGUS) under the Bethesda System of terminology, the instant methods are still identical and the type of cells or samples they are performed on does not patentably distinguish the methods (See entire document, including figures)

Furthermore although Liao et al. fails to teach detection in Pap smears, this would be an obvious variation, because it is well known in the art that Pap smears are the standard method of monitoring cervical cells and testing for cervical dysplasia and carcinoma.

Therefore it would have been *prima facie* obvious to use the method of Liao et al. on pap smears and one would have been motivated to do so because pap smears are the art standard method of diagnosis and monitoring for cervical dysplasia and cancer.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Nichols, whose telephone number is (703) 308-7548. The examiner can normally be reached Monday through Thursday 6:30am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached at (703) 308-3995. The fax number for the group is (703) 305-3014 or (703) 308-4242.

Communications via internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [**anthony.caputa@uspto.gov**].

All internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists the possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the group receptionist, whose telephone number is (703) 308-0196.

Jennifer Nichols, Nee Hunt

August 26, 2000

Brenda Brumback

BRENDA BRUMBACK
PATENT EXAMINER